REMARKS

Claims 1-2, 6-9, and 11 are pending in this application. Claims 3-5, 10 and 12-88 are canceled without prejudice to further prosecution in a related application(s).

Claim Objections

Claim 11

Claim 11 was objected to for failing to spell out the abbreviation "hCF (SC20)". Claim 11 has been amended to recite the "transchromosome SC20" to address this objection. This amendment finds support in the specification on page 4, lines 11-12.

Claim Rejections

35 USC §112, first paragraph

Claims 1-4, 6-11

Claims 1-4 and 6-11 were rejected under 35 USC §112, first paragraph for failing to provide enablement commensurate with the scope of the claims. Specifically, the Examiner asserted that the specification does not enable the making of any transgenic mammal other than the exemplified transgenic mouse. Without addressing the propriety of the rejection, the Applicant has amended the claims to recite only a transgenic mouse. Claim 3 has been canceled in view of the amendments to Claim 1. Claims 4 and 10 also have been canceled as they were directed toward subject matter which is now claimed in other pending claims. Claim 9 has been amended to specify a transgenic mouse which comprises the KCo5 transgene.

The Applicant submits that the amended claims are enabled by the specification and the general knowledge in the art at the time of filing. Amended Claim 1 recites a transgenic mouse comprising two human immunoglobulin loci, wherein one of the human immunoglobulin loci is a human heavy chain locus and the other locus is a human light chain locus, and wherein the human heavy chain locus is carried by a transchromosome having a centromere of human chromosome 14 and the human light chain locus is carried by a transgene integrated into the genome of the mouse.

The specification, most particularly in the Examples, sets forth the protocol for obtaining such a mouse. One of skill in the art would understand that the protocol used to generate the hCF(SC20)/KCo5 mouse exemplified in the specification could be used to generate transgenic mice containing other transgenes and transchromosomes carrying human immunoglobulin loci.

The Examiner also asserts that chromosomal transfer is unpredictable, citing Green, US 2003/0093821 and Tomizuka (PNAS 2000). However, the present invention, particularly the claims being examined, are not concerned with efficiency of transchromosomal transfer but rather with combining a stable, transmittable transchromosome comprising the human heavy chain locus with a transgene comprising the human light chain locus in order to improve the stability of the light chain locus as compared to the human antibody producing mouse described in Tomizuka (PNAS 2000). The improved properties of the animals of the invention are described in the specification in, for example, Examples 5, 6, and 7. Furthermore, as noted in the specification on page 39, line 32, through page 40, line 16, numerous transgenic mice carrying human immunoglobulin light chain transgenes (other than KCo5) and expressing human antibodies had been generated by the time of filing the instant specification. Applicant asserts that the claims, as amended, are fully supported by the specification in view of the knowledge of those skilled in the art of the production of transgenic mice.

Claim 1

Claim 1 was rejected under 35 U.S.C. §112, first paragraph for failing to provide enablement commensurate with the scope of the claims. Specifically, the Examiner rejected Claim 1 for failing to teach how one of the claimed loci is not of a transchromosome. Applicant has amended Claim 1 to remove the phrase "of a transchromosome". Amended Claim 1 recites a transgenic mouse comprising two human immunoglobulin loci, wherein one of the human immunoglobulin loci is a human heavy chain locus and the other locus is a human light chain locus; and wherein the human heavy chain locus is carried by a transchromosome having a centromere of human chromosome 14 and the human light chain locus is carried by a transgene integrated into the genome of the mouse.

Thus, the claims now specify that the transchromosome contains a centromere and the transgene is integrated into the genome of the mouse. Support for the amendment can be found on page 38, line 13, through page 39, line 23, and in Example 2. Applicant asserts that Claim 1 as amended is in compliance with 35 U.S.C. §112, first paragraph. Claim 11 has been amended to conform to the language of amended Claim 1.

Claims 4 and 8

Claims 4 and 8 were rejected for first paragraph for failing to provide enablement commensurate with the scope of the claims. Specifically, the Examiner rejected Claims 4 and 8 stating that the present specification fails to teach how to transfer a YAC vector containing only part of a locus into a cell and fails to teach how the YAC will definitely be integrated into the endogenous genome as desired.

This rejection has been rendered moot with respect to claim 4 in view of its cancellation.

Applicant respectfully traverses this rejection as it applies to Claim 8. Claim 8 is directed to a transgenic mouse wherein at least part of the light chain locus carried by the transgene integrated into the mouse genome is cloned into a YAC vector. Example 2 of the specification sets forth a procedure using a YAC vector comprising a portion of the human V kappa locus to generate the human kappa light chain transgenic mouse line KCo5-9272. Additionally, the use of YAC vectors to introduce genes, or portions of genes, into the genome of a host organisms was well-known at the time of filing the instant application. For example, see the list of references cited on page 39, line 32, through page 40, line 5, of the instant specification and incorporated by reference. The Examiner cites the *Nielson* reference as showing that the YAC vector does not always integrate into the host genome. However, *Nielson* is concerned with specific YAC vectors, such as pYACneo, modified to contain human origins sequences that promote autonomous replication in human cells. *Nielson* is not applicable to the YAC vectors used to generate transgenes that are integrated into the host mouse genome. Applicant asserts that Claim 8 as amended is in compliance with 35 U.S.C. §112, first paragraph.

35 USC §112, second paragraph

Claims 1-4 and 6-11

Claim 1, and claims dependent thereon, was rejected under 35 USC §112, second paragraph for failing to particularly point out and distinctly claim the subject matter the applicant regards as the invention. Specifically, the Examiner asserts that Claim 1 is vague and indefinite because Claim 1 recites a transgenic nonhuman mammal comprising two human immunoglobulin loci...wherein only one of said loci is of a transchromosome. Applicant has amended the claims to remove the phrase "of a transchromosome". Amended Claim 1 recites a transgenic mouse comprising two human immunoglobulin loci, wherein one of the human immunoglobulin loci is a human heavy chain locus and the other locus is a human light chain locus; and wherein the human heavy chain locus is carried by a transchromosome having a centromere of human chromosome 14 and the human light chain locus is carried by a transgene integrated into the genome of the mouse. Thus the claims now specify that the transchromosome contains a centromere and the transgene is integrated into the genome of the mouse. Support for the amendment can be found on page 38, line 13; through page 39, line 23 and in Example 2. Applicant submits that Claim 1, and claims dependent thereon, are not vague and indefinite..

The claims were rejected as being vague and indefinite because of the claim recitation "locus associated with an endogenous mammalian chromosome." None of the currently pending claims recite this claim language and thus Applicant asserts that this rejection is no longer applicable.

Claim 6 was rejected for lack of antecedent basis for the term "the endogenous mammalian heavy chain locus". Applicant has amended Claim 6 to replace the term "the endogenous" with the term "an endogenous". Applicant believes this amendment addresses the Examiner's concerns regarding antecedent basis.

Claim 6 was rejected as being vague and indefinite for reciting "at least one mammalian light chain locus" while not clarifying which mammalian locus is meant. Applicant has amended Claim 6 so that it specifies "at least one endogenous mouse light chain locus" is inactivated. Applicant

submits that amended Claim 6 is not vague and indefinite. Claim 7 has been similarly amended to specify that the inactivated kappa light chain is the endogenous mouse kappa light chain.

Claim 11 was rejected as being vague and indefinite for use of the term (SC20), which the Examiner characterizes as a custom-term not defined in the specification. Applicant respectfully disagrees with the rejection. As the Examiner is aware, the Applicant is free to act as his own lexicographer as long as the meaning of any term used is defined in the specification. The term SC20 is clearly defined in the specification. For example, as set forth in Example 3, SC20 denotes a particular fragment of human chromosome 14 carrying the human heavy chain locus. The identity of SC20 is further discussed throughout the Examples, especially Example 3, and is also presented in the reference Tomizuka, K. *et al.*, 2000, *Proc. Natl. Acad. Sci. U.S.A.* 97:722-727, which was incorporated by reference in the present specification. Additionally, a cell line containing the SC20 transchromosome has been deposited in the International Patent Organism Depository, National Institute of Advanced Industrial Science and Technology, Japan, Depository number FERM BP-7583, with the assigned designation of SC20. Accordingly, Applicant submits that use of the term SC20 does not render Claim 11 vague and indefinite.

Conclusion

Applicant respectfully submits that the claims are now in condition for allowance. If upon, review, the Examiner feels there are additional outstanding issues, the Examiner is invited to direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY LLP

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Traci H. Ropp
Reg. No. 44,307

Four Embarcadero Center, Suite 3400
San Francisco, California 94111-4187
Telephone: (415) 781-1989
1119326

Customer Number 32940